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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/679,699	10/02/2003	David Bar-Or	4172-85	2007

22442 7590 02/28/2008

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EXAMINER	
EMCH, GREGORY S	
ART UNIT	PAPER NUMBER
1649	
MAIL DATE	DELIVERY MODE
02/28/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/679,699	BAR-OR ET AL.	
	Examiner	Art Unit	
	Gregory S. Emch	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *47-54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *47-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *06/02/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicants' submission filed on 03 December 2007 has been entered.

Response to Amendment

No claim amendments were made in the reply filed on 03 December 2007. Currently, claims 47-54 are pending and under examination in the instant office action.

Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicants' response and withdrawn.

Information Disclosure Statements

A signed and initialed copy of the IDS paper filed 02 June 2007 is enclosed in this action.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 47-54 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of diagnosing multiple sclerosis wherein the biological sample is serum, plasma or blood, does not reasonably provide enablement for the claimed method of monitoring multiple sclerosis or for the claimed method of diagnosing MS with any biological sample. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and, (8) the breadth of the claims. *In re Wands*, 8 USPQ2d, 1400 (CAFC 1988).

In the reply filed on 03 December 2007, Applicants assert that because the Jara et al. reference teaches His-Pro-DKP, it is not relevant to the instant claims because said claims encompass DA-DKP, NAS-DKP, and compounds with masses of 175 and 145. Applicants also assert that the Jara et al. reference only teaches that His-Pro-DKP is present in serum. Applicants allege that those skilled in the art could readily determine how to detect markers in any bodily fluid and correlate said markers to MS or

active MS, since such methods are well known in the art and are described in the specification.

Applicants' arguments have been fully considered and are not found persuasive.

Applicants' assertion that the Jara et al. reference teaches that His-Pro-DKP is present only in serum is inaccurate. As stated previously, the Jara et al. reference teaches that DKPs are distributed in a variety of body fluids, including plasma, serum, cerebrospinal fluid, and urine and in a variety of tissues, including brain, gut and skin (see p.259, col.2). Further, although the prior art teaches that His-Pro-DKP is present in a number of tissues/biological samples, the art is silent with respect to the claimed biomarkers. Thus, art that concerns His-Pro-DKP is the closest prior art and is not irrelevant. Absent evidence to the contrary, the claimed DKPs would also be expected to be present in a variety of tissues as the structure of the core molecule (diketopiperazine) is conserved in Applicants' claimed embodiments and in those of the prior art.

Moreover, although one of skill in the art would know how to measure a generic biomarker in a generic biological sample, neither the art nor Applicants' specification enables methods of diagnosing MS with the claimed biomarkers in any biological tissue. The claimed biomarkers, i.e., those with a mass of 175 and 145 are described only in terms of mass and can encompass a multitude of undisclosed compounds. The claimed "biological sample" is generic to not only those mentioned above but can encompass e.g., hair, skin, nervous tissue, organ tissue, etc. These variant biological samples encompass an enormous number of compounds that potentially have the

same mass of 175 and 145. Moreover, the state-of-the-art establishes that diagnostic markers for MS are measured in some biological samples (i.e., serum, plasma, blood and CSF) but not in others (see Rinaldi et al. Neurol Sci. 2005 Dec;26 Suppl 4:S215-7 and Kuenz et al. J Neuroimmunol. 2005 Oct;167(1-2):143-9). Thus, Applicants are only enabled for measuring these compounds and correlating them to MS status in blood, serum or plasma as taught by the examples disclosed in the instant specification.

Applicants' data in the specification provides a correlation between the claimed markers and patients diagnosed with MS in a small sample size. Applicants have provided no data regarding the claimed embodiment of monitoring MS disease. Again, the art does not provide compensatory teachings as it is completely silent with regards to this embodiment. Thus, there is no nexus established between Applicants' data and monitoring of MS.

The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without such guidance, the changes which can be made and still maintain activity/utility is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Int. 1986).

The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. Due to the large quantity of experimentation necessary practice the claimed method of monitoring MS or of diagnosing MS with any biological sample, given the lack of direction/guidance

presented in the specification, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the claimed methods, and the breadth of the claims which encompass methods of diagnosing or monitoring MS in any bodily fluid or tissue sample, undue experimentation would be required of the skilled artisan to practice the claimed invention commensurate in scope with the claims.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gregory S. Emch whose telephone number is (571) 272-8149. The examiner can normally be reached 9:00 am - 5:30 pm EST (M-F).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey J. Stucker can be reached at (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Gregory S. Emch/

Gregory S. Emch, Ph.D.
Patent Examiner
Art Unit 1649
06 February 2008

/Elizabeth C. Kemmerer/
Primary Examiner, Art Unit 1646